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Title: Towards refined environmental scenarios for ecological risk assessment of down-the-drain chemicals in freshwater environments

Running head: scenario-based ecological risk assessment

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Abstract

Current regulatory practice for chemical risk assessment suffers from the lack of realism in conventional frameworks. Despite significant advances in exposure and ecological effect modelling, the implementation of novel approaches as high tier options for prospective regulatory risk assessment remains limited, particularly among general chemicals such as down-the-drain ingredients. While reviewing the current state of art in environmental exposure and ecological effect modelling, we propose a scenario-based framework that enables a better integration of exposure and effect assessments in a tiered approach. Global- to catchment-scale spatially explicit exposure models can be used to identify exposure hotspots and to generate ecologically relevant exposure information for input into effect models. Numerous examples of mechanistic ecological effect models demonstrate that it is technically feasible to extrapolate from individual-level effects to effects at higher levels of biological organisation and from laboratory to environmental conditions. However, the data required to parameterize effect models that can embrace the complexity of ecosystems are large and require a targeted approach. Experimental efforts should, therefore, focus on vulnerable species/traits and ecological conditions of relevance. We outline key research needs to address the challenges that currently hinder the practical application of advanced model-based approaches to risk assessment of down-the-drain chemicals.

Keywords

Environmental scenario, ecological risk assessment, down-the-drain chemicals, spatial models, ecological models

1. INTRODUCTION

The lack of ecological realism is a widely recognised limitation in current regulatory practice for chemical risk assessment. The conventional prospective risk assessment paradigm based on the ratio between predicted environmental concentrations (PECs) (calculated for worst-case exposure scenarios) and predicted no effect concentrations (PNECs) (generally extrapolated from individual-level laboratory toxicity data for a few standard test species), provide some evidence of ecological risks but is aimed at being protective rather than predictive. In countries where chemical regulation is established protection goals are often vaguely defined and a precautionary approach is usually taken to translate them into conservative safety thresholds (Hommen et al. 2010). In Europe, such regulatory inadequacies have been highlighted (SCENIHR et al. 2012). Three key scientific challenges have been identified to achieve better informed risk management decisions from environmental risk assessments: i) the definition of relevant protection goals matching societal needs, ii) the development of relevant, spatially explicit exposure assessment tools, and iii) the development of mechanistic effects models (Price and Thorbek 2014). These challenges are interdependent and need to be addressed using an integrated approach. For example, the life-cycle characteristics of vulnerable organisms can inform the spatial-temporal resolution required for higher tier exposure modelling when effect and recovery evaluations are performed at the individual or population level. The values of environmental parameters used in exposure assessments may not correspond with realistic worst-case conditions from an ecological perspective, thus resulting in a potential mismatch between the predicted exposure and the ecological scenario that is represented in a risk assessment (Rico et al. 2015). To address this, we envisage a pragmatic and flexible framework to derive environmental scenarios for risk assessments tailored for the specific chemical emission and exposure profile, the

ecotoxicological mode(s) of action, and the biological entities to be protected (e.g. individuals, populations) derived from established protection goals.

Aquatic ecosystems receiving treated or untreated domestic wastewater are typically exposed to low concentrations of a wide range of chemicals, such as ingredients of home and personal care products or pharmaceuticals, resulting from continuous emissions from point sources. Although emissions of these types of ‘down the drain’ chemicals can be considered relatively constant in time, exposure is variable in space and time due to seasonal variations in river flows, the removal efficiency of sewage treatment plants and use and disposal patterns. Other water quality stressors associated with wastewater (e.g. BOD, ammonia, nitrate, nitrite, suspended solids) are likely to represent an important threat to an ecosystem’s health, particularly downstream of untreated wastewater discharges (Finnegan et al. 2009). In such a scenario, the ecological consequences of exposures exceeding a PNEC value derived to protect all species may or may not be a concern due our limited understanding of ecosystems’ baseline structure and function and of combined effects of multiple stress factors. Alternative protection goals have been proposed for a generic direct discharge scenario (Finnegan et al. 2009).

Ecological effect models have been proposed to extrapolate from responses observed for individuals in laboratory toxicity tests to expected effects on populations (see Galic et al. 2010 for a review). Such models have also been designed to address effects on communities and to integrate multiple stressors typically present in real ecosystems, but have primarily been developed for pesticides (Galic et al., 2010). For most household use chemicals, significant gaps exist in the chronic ecotoxicological datasets, the low concentration nature of which is most relevant to the continuous, low levels of exposure in aquatic systems resulting from wastewater discharge. Our understanding of population/community level responses (including direct and

indirect effects and recovery potential) to chemicals in multi-stressed freshwater ecosystems is also limited (Baird et al., 2015).

In Europe, research efforts are being made to incorporate aspects of ecological relevance in prospective chemical risk assessment of down-the-drain chemicals (De Laender et al., 2014a; Forbes et al., 2011; Lombardo et al., 2015), focusing on scenarios representative of developed regions. In developing regions, where the ecological status of freshwater bodies is often characterised by poor water quality resulting from direct discharge of untreated wastewater, the need to improve the ecological realism of chemical risk assessment is equally compelling. The lack of a systematic approach to defining environmental scenarios, and in particular the ecological component of such scenarios, hinders the application (and regulatory acceptance) of ecological effect models in risk assessment. The need to develop realistic ecological scenarios for higher tier risk assessment has been recently recognised with the development of ecological models for risk assessment and the definition of acceptance and evaluation criteria (Augusiak et al. 2014; EFSA 2014). Realistic but generalized scenarios which are representative of different geographies are needed to parameterise models that are able to integrate exposure and effects in a prospective risk assessment framework. In this paper we propose a stepwise strategy to develop and implement environmental scenarios in a framework suitable for down-the-drain chemicals.

2. ENVIRONMENTAL SCENARIOS

In the regulatory risk assessment of chemicals, an environmental scenario can be defined as the conceptual and quantitative description of the environmental context relevant to the risk assessment (EFSA 2014). An environmental scenario is comprised of two fundamental components, the exposure scenario and the ecological scenario (Rico et al. 2015; Figure 1).

Standardized exposure scenarios have been used for many years in regulatory frameworks and are widely accepted by stakeholders (e.g. the FOCUS scenarios for pesticides; FOCUS, 2011 and the European Union system for the Evaluation of Substances (EUSES) scenarios for general chemicals; Vermeire et al. 2004). Conceptually, an exposure scenario is defined by its spatial and temporal scale and by a qualitative description of the environmental context it represents. For example, in EUSES, the regional scale exposure scenario is a steady-state representation of a generic 200×200 km densely populated, industrialised European region. In quantitative terms, exposure scenarios are developed by choosing the spatio-temporal resolution and by assigning parameter values in a given mathematical modelling framework, typically including an emission and an environmental fate component. For screening risk assessment purposes, such parameterisation is often based on a realistic, worst-case situation. The emission component of the exposure scenario, often referred to as the emission scenario, consists of the assumptions about chemical use, consumer habits, disposal pathways, and wastewater treatment infrastructure. The environmental fate component of the exposure scenario corresponds to the parameterisation of all abiotic and biotic factors that influence the environmental fate and dissipation of chemicals in the modelled environmental compartments.

The conceptual description of the ecological context relevant to conventional risk assessment frameworks can be defined loosely as the entire pool of species potentially present in a given geographical context. Indeed, in contrast to exposure scenarios, ecological scenarios are far less well defined. In aquatic risk assessment down-the-drain chemicals, the number of tested species is limited in most cases to three species, representing different trophic levels (algae, daphnia and fish), chosen primarily for practical reasons, such as ease of culture. The experimental lab conditions of standard toxicity tests (i.e. controlled medium composition, temperature, optimal

food availability, no predation etc.) are poorly representative of realistic ecological conditions (Van den Brink, 2008). The characterisation of an ecological scenario should relate to the natural factors influencing the biological integrity of the ecosystem (e.g. climate, river morphology, water quality) as well as to the specific stress to be evaluated, in our case chemical stress. Rico et al. (2015) defined ecological scenarios as the combination of biotic and abiotic parameters influence chemical-induced effects and recovery of populations. In prospective risk assessment, a vulnerability-based ecological scenario can be defined as a realistic worst-case representation of such parameters. The biotic parameters that define the scenario should describe the taxonomic composition along with the biological characteristics or traits influencing organism-level sensitivity, recovery potential and propagation of effects to higher levels of biological organisation through indirect effects (Rico et al., 2015). Examples of biological traits influencing toxicant effects at the individual level include respiration type, size, life cycle duration or degree of sclerotization (Baird and Van den Brink 2007; Rubach et al. 2012; Rico and Van den Brink 2015). Examples of biological traits influencing the resilience and the ability of of populations and communities to recover include the reproductive characteristics and recolonization ability of the disturbed populations (Gergs et al. 2016; Rico and Van den Brink 2015), the trophic state of the exposed system (oligo- or eutrophic; Alexander et al. 2013; De Hoop et al. 2013; Gabsi et al. 2014), the strength of inter- and intraspecific species interactions in a food-web context (e.g. predation, competition; De Laender et al. 2015) and the complexity of this food-web (De Laender et al. 2015). In the context of ecological effect modelling, it has been proposed to define an ecological scenario by allocating one value to each variable potentially influencing population- and ecosystem-level responses to a (mixture of) chemical(s) (De Laender et al. 2015).

An accurate selection of the key abiotic parameters of an environmental scenario should facilitate the integration of exposure and effects modelling because exposure and ecological scenarios share a number of important variables, e.g. temperature or trophic state influence both exposure and effects (De Laender et al. 2015; Morselli et al., 2015). Therefore, it has been proposed to integrate both into ‘environmental scenarios’ and to define them using a combination of biotic and abiotic parameters (and input values), which result in a realistic worst-case representation of the exposure, effects and recovery of the biological entities that we intend to protect (Rico et al. 2015). Such unification of exposure and ecological scenarios ensures consistency in the consideration of those variables that influence both exposure and effects. For example, temperature may influence exposure concentrations through temperature-dependent degradation kinetics, but it may also influence the population response through temperature-dependent growth kinetics (Heugens et al. 2006). Other parameters that may affect both exposure and effects include flow velocity, concentrations of suspended and dissolved solids, suspended and dissolved organic matter, nutrients, pH, as well as landscape features such as the connectivity of exposed and non-exposed habitats and the presence of refugees (e.g. Traas et al. 2004). One of the major challenges in the unification of exposure and ecological scenarios is the selection of the suitable spatio-temporal scales that can adequately represent realistic worst-case combinations of exposure (e.g. low flow season) and ecological scenarios (e.g. sensitive life stages). Compared to chemicals characterized by as pulse input exposure at certain points in time corresponding to specific life stages in seasonal organisms, the consideration of spatio-temporal scale for down-the-drain chemicals is somewhat facilitated by the (semi)continuous nature of down-the-drain chemical emissions.

3. DEVELOPMENT OF ENVIRONMENTAL SCENARIOS IN A TIERED RISK ASSESSMENT FRAMEWORK

There are two important considerations in accounting for spatial and temporal variation in biotic and abiotic characteristics of ecosystems for chemical risk assessment. One is in defining specific protection goals (SPGs) for different spatial units and the other is in developing exposure and toxicity assessment methods and models that predict safe thresholds for the ecological entities in the environmental scenarios.

The current regulatory approach of protecting all species everywhere, all of the time, is likely to be overly conservative in locations where the more sensitive taxonomic groups do not occur. As an alternative to this approach, SPGs could be used to provide guidance for the selection of the biological entities and spatio-temporal dimensions that the scenarios should address. Defining SPGs could either be achieved by applying the top-down ecosystem services concept or by use of the bottom-up empirical characterisation of scenarios with representative ecological community structures and functions derived from biomonitoring or survey data. Both approaches are suitable for chemicals in home and personal care products when higher tier refinement of generic approaches is needed, i.e. for high volume chemicals with small safety margins. The advantage of using ecosystem services to set SPGs for environmental scenarios is that the approach facilitates the identification of key service-providing traits or taxonomic units (Nienstedt et al. 2012) which can be aligned to service-related water management objectives, e.g. fisheries, flood protection, amenity value.

The implementation of SPGs in prospective risk assessment requires the identification of reasonable worst case environmental scenarios as well as quantitative descriptions of acceptable/unacceptable impacts on biological entities so that toxicity testing and ecological

modelling can be suitably designed. Conventional endpoints measured in standard toxicity tests (e.g. LC_{50} or EC_{50}) refer to impacts defined at an individual organism level and the safety threshold is derived via the use of default assessment factors to account for extrapolation from individual-level endpoints to higher levels of biological organisation (as well as other uncertainties e.g. differences in species intrinsic sensitivity) (Homment et al. 2010). Whilst this approach lacks mechanistic rationale, it is simple and easy to apply. Further research is needed to better define how to derive chemical concentrations thresholds which are protective of different SPGs. Because SPGs refer to the structural and functional health of defined environmental typologies, they are better described by the integrity of species populations or, for groups of species with similar functional roles in the ecosystem (e.g. microorganisms), by the integrity of functional roles. Therefore, in this paper we assume that ecological scenarios and models will target the population level of biological organisation. However, a thorough evaluation and a consensus on which SPGs should be applied in the prospective risk assessment of down-the-drain chemicals is still to be reached,

3.1 Towards spatially explicit exposure scenarios

In the lower tiers of regulatory risk assessment of home and personal care chemicals the exposure scenario consists of a zero-dimensional unit environment. The Mackay-type steady-state multimedia box models have proved a convenient platform to reflect the multi-media nature of potential chemical emissions, transport and removal pathways. A key reason for the widespread use of these models is the simplicity of the model structure and, probably more importantly the simplicity of the model outputs (a single PEC estimate for each environmental compartment), which facilitates easy use in risk assessment and decision-making. Single-box

multimedia fate models can also be used to identify the most sensitive input parameters that influence exposure (Figure 1). For example, sensitivity and uncertainty analysis of multimedia box models have shown that chemical emissions and hydrological parameters (determining dilution) are essential inputs independent of chemicals' properties, while other inputs and model parameters such as biodegradation rates, temperature, organic matter content and pH can be important depending on the physicochemical and environmental fate properties (Ying et al. 2014). Multimedia box models used in regulatory frameworks for general chemicals (e.g. REACH) are, however, limited to one box per region/continent and one set of landscape characteristics per box and cannot account for highly spatially differentiated or localised emissions and exposure pathways. Under other chemical regulations, bespoke local-scale scenarios have been developed to represent the specific use settings of different product types (e.g. biocides) or regional-specific landscape and climatic properties (e.g. pesticides; FOCUS, 2001). The lack of spatial resolution is a major limitation for predicting accurate exposures of down-the-drain chemicals, for which exposure is extremely variable within and across freshwater catchments.

Large-scale spatially explicit environmental fate models can play a key role in the identification of catchments or river section hotspots of exposure. Different spatially explicit models have been developed to cover higher resolution assessment of rivers on a catchment or continental scale. For example, the in-STREam Exposure Model, iSTREEM, is designed to evaluate exposure of chemicals in down-the-drain products (Aronson 2014). It predicts concentrations in over 28,000 river reaches representing over 200,000 river miles resulting from discharges from over 10,000 wastewater treatment plants across the continental United States. Removal by wastewater treatment plants is accounted for by the model, concentration being

primarily determined by dilution and a simple constant in-stream removal rate that does not depend on river characteristics. GREAT-ER has been developed as a geo-referenced model for high tier exposure assessment (Kehrein et al., 2015) and has been used to simulate the fate and exposure of down-the-drain chemicals in whole watersheds (Price et al. 2009). However, data requirements for parameterisation of such models are not readily available at continental or global scales. A major limitation of these approaches is the lack of the multi-media transport component to describe atmospheric and terrestrial pathways (e.g. sludge application to soil, irrigation, and volatilisation). Recent developments in the prediction of spatial emissions over entire continents (ScenAT model, Hodges et al. 2012) have made it possible to determine large, highly resolved variations in use and subsequent discharges of chemicals in home and personal care products. The ScenAT model is based on demographic (e.g. population density) and economic indicators (e.g. per capita GDP), and can differentiate between treated and untreated wastewater discharges. ScenAT uses market research data on product sales, as a proxy for usage which, when combined with ingredient inclusion levels, can be used to predict regional differences in consumption of home and personal care products. Furthermore, when coupled with high resolution population or economic activity data, it is possible to project usage of products and/or ingredients at 1 km resolution. Hodges et al. (2012) go further by linking usage with spatially resolved information on water use and household wastewater treatment technologies.

Projections of chemical consumption (e.g. from product consumption and chemical inclusion levels in formulations) and emissions to the environment can be used as input to spatially refined multimedia fate models. A first step is the definition of region specific parameterization of nested multi-media models, as performed for USEtox for different regions of the world (Kounina et al., 2014). Spatial multimedia fate models have also been developed at a

2° by 2.5° (approximately 200x200 km at temperate latitude) resolution for entire continents (Humbert et al., 2009) but such a resolution is not sufficient to analyse spatial variations in down-the-drain chemicals. The multi-scale multimedia fate and exposure model Pangea offers the unique ability to create multi-scale grids and project spatial data onto these grids at runtime (Wannaz et al., 2015). A GIS engine based on ArcGIS is used in the Pangea model to produce 3-dimensional multi-scale grids, covering all relevant environmental media, to project spatial data sets and to compute geometric and topological parameters. This process yields a geometric system of connected grid cells associated with a set of proportions of relevant media within each grid cell. Terrestrial cells, for example, may be composed of several types of land cover and freshwater. This multi-scale, flexible parameterization can predict concentrations at the global scale, with refinement of the grids to a higher resolution only for relevant areas of interest (e.g. exposure hotspots). The routed hydrological component of the model is currently based on the gridded 0.5°× 0.5° water network (about 50×50 km) and annual average flows defined by the World Water Development Report II (Vorosmarty et al., 2000a and 2000b) and its adaptation by Helmes et al. (2012). On the global scale, a promising alternative to further refine the hydrological parameterisation is based on the HydroSHEDS dataset and the HydroROUT model (Lehner and Grill 2013), which offers the possibility of refining the hydrological network with a sub-kilometre resolution. Data and attributes calculated by HydroSHEDS for each of the 12 complementary resolutions include annual discharge, flow direction, average depth and surface area of river and lakes and can be used for the model parameterisation at each resolution. Although such an approach is applicable on a global scale for the hydrological parameterisation, highly spatially refined exposure scenarios are only meaningful if all sensitive model inputs and environmental parameters can be refined to a similar level of resolution. For many factors

affecting emissions (e.g. chemical use, wastewater infrastructure), environmental fate and bioavailability (e.g. particulate and dissolved organic matter) (Figure 1) this is only feasible on a limited number of site-specific catchment scenarios due to data availability or, more practically, to manage model complexity. Specific scenarios can be selected based on large scale simulations to identify exposure hotspots and/or based on the availability of existing data for parameterisation. Crucially, a robust global scale model framework enables characterisation of the significance of a chosen catchment scenario in the context of risk assessment over large regions (e.g. a 90%-ile worst-case catchment scenario in a given region). High resolution (sub)catchment-scale scenarios need to be defined to develop and evaluate models for higher tier exposure assessments. The validity of the steady-state assumption, which may be acceptable at lower to mid-tier assessment levels given the (semi)continuous nature of down-the-drain chemical emissions, needs to be reconsidered. Changes in hydrological regime and for some product types seasonality in emissions (e.g. higher use of pharmaceuticals in winter or of sunscreens in summer) result in temporal variability in exposure. Seasonal low flow conditions are associated with lower dilution and therefore higher exposure (Grill et al 2016). In addition to hydrological considerations, higher tier exposure models should incorporate a refined parameterisation of factors affecting bioavailability, such as the fluxes, concentration and organic matter content of suspended and dissolved. All these parameters can be highly dynamic, implying significant deviations from steady-state exposure. Sediments transport increases dramatically during high flow events (Dale et al. 2015). Organic matter content varies with seasonal cycles of primary and secondary production, particularly in slow flowing lentic systems (Morselli et al. 2015). Exposure models built on specific catchment scenarios should carefully address these aspects to provide a realistic exposure input data layer at a suitable resolution for

ecological effect modelling. At this scale, a coherent parameterisation of the abiotic and biotic factors relevant to both exposure and effects (Figure 1) is required to fully merge the exposure and the ecological scenario into integrated environmental scenarios, reducing the mismatch in the spatio-temporal scale and parameterisation between exposure and effect assessment (Figure 1). Regardless of the model design, freely dissolved concentration should be the common metric at the interface between exposure and effect assessment because it reflects external exposure as seen by organisms. Examples of exposure scenarios of simple lotic systems designed for the integration of exposure and ecological models demonstrated the importance of spatio-temporal resolution in particulate and dissolved organic matter driven by seasonal dynamics in ecosystem primary productivity, on water-dissolved concentrations (Morselli et al. 2015).

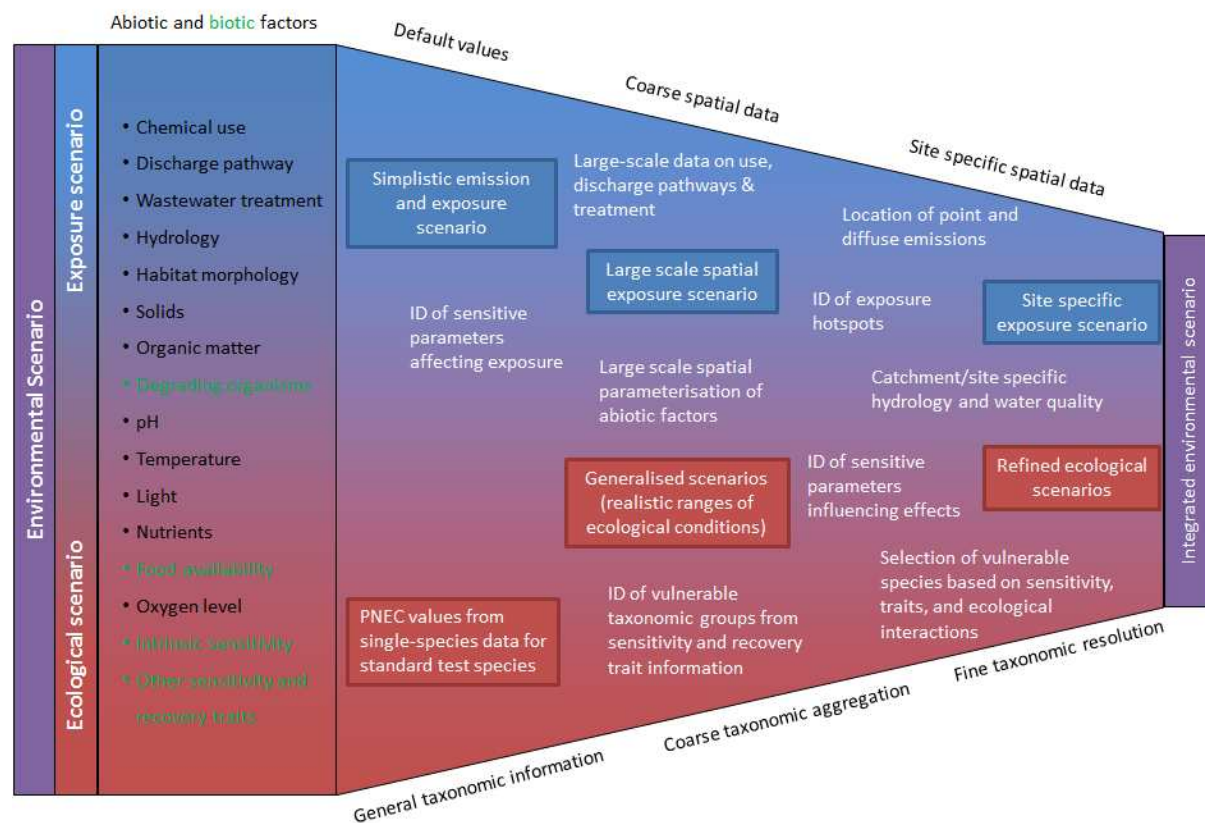


Figure 1. Development of environmental scenarios from lower to higher tier risk assessment. Key factors are incorporated at increasing spatial-temporal resolution (exposure scenario) and taxonomic resolution (ecological scenario) towards integrated exposure and ecological scenarios (environmental scenarios) for specific combinations of realistic worst-case catchment and vulnerable taxa.

3.2 Vulnerability-based ecological scenarios

Characterisation of ecosystem type

An initial step towards the development of realistic worst-case scenarios is the characterisation of ecosystems in typical/standard water body types that may be exposed to down-the-drain chemicals. This exercise can be done *a priori* and does not require any chemical-specific information. In temperate and humid zones, typical fresh water bodies receiving domestic wastewater discharges mainly consist of lotic ecosystems, ranging from minor urban streams to medium and large lowland rivers. Lentic ecosystems such as lakes, ponds or lagoons can also be an important scenario in certain regions. In regions with poor wastewater infrastructure, untreated wastewater is often discharged to artificial open drainage channels before reaching natural ecosystems. In (semi)arid regions, wastewater is often discharged to ephemeral water bodies or even reused directly or after treatment for groundwater recharge, irrigation, or urban landscaping. Large-scale data on the emission scenario, such as the type of household drainage system, local or centralised wastewater treatment infrastructure can help characterise the typology of ecosystems to be assessed (Figure 1). Data need to be collected at scales relevant for the size of the aquatic system, including the main habitat parameters that determine the ecological status in taxonomic and functional terms such as flow velocity,

hydrological regime, depth, light intensity, temperature, geological substrate, trophic status and chemical water quality. Continental-scale assessments of freshwater habitat typologies (EEA 2014) and pressures (EEA 2012) provide a valid data source.

Taxonomic and traits-based description of aquatic communities

A second step would be to describe the community of each ecosystem type based on taxonomy and traits. The description of communities based on the taxonomy and the subsequent transformation into trait characteristics can be achieved by compiling available information on the structural composition of those communities in the represented water bodies. For this, ecological monitoring surveys such as those used for the evaluation of the ecological status of the European water bodies as part of the Water Framework Directive (WFD) can be of great help. A challenge in interpreting these data will be the selection of representative ecosystems that are not impacted by chemical or physical anthropogenic stressors. The selection of datasets for river transects or other water bodies that are considered to be reference ecosystems for the derivation of Environmental Quality Standards in the eco-regions established as part of the WFD intercalibration exercise (Borja et al. 2007) could be used in the derivation of taxonomic collections that represent ecosystems unaffected by major environmental stress. Because species composition is likely to vary across sub-continental scales, the description of aquatic communities in terms of their biological traits would increase the generality of such characterizations and subsequent transferability between scenarios (Van den Brink et al., 2011). The taxonomic information could be transferred into trait-based descriptions using available trait databases for aquatic organisms (e.g. Poff et al. 2006; Usseglio-Polatera et al. 2000). Traits can be constant for all individuals (e.g. basic life stages, degree of sclerotization etc.) changing over

a lifetime (i.e. those that are plastic. e.g. size, lipid content). Accounting for intraspecific variability of traits combinations, as often reported in existing databases, will increase the realism and relevance of the scenarios and may prevent overestimation of impacts on community composition (De Laender et al. 2014b).

Habitat filtering can be applied to predict the presence of species with competitive traits under a combination of environmental factors, including natural and anthropogenic stressors (e.g. Kearney and Porter 2009; Kearney et al. 2010). Due to the co-occurrence of multiple water quality stressors in effluent discharge areas (e.g. oxygen depletion, ammonia, nutrient, chemical mixtures) different filters can be applied to an initial pool of all potential species to establish baseline conditions in the absence and in the presence of anthropogenic (but non chemical) stress. In this way it will be possible to assess the impact of chemical(s) stress under realistic conditions. If unstressed baseline conditions cannot be established (i.e. due to widespread contamination from wastewater discharges), ecological scenarios for impacted ecosystems may be the only feasible baseline. In such situations, however, it will be difficult to unravel the effects of chemicals' stress as compared to other wastewater stressors.

Selection of vulnerable taxa

The 'population vulnerability' concept developed by Van Straalen (1994) considers three factors affecting the vulnerability of populations: likeliness of exposure (organism-level), intrinsic sensitivity (organism-level) and population sustainability (population-level); later Van den Brink (2008) added indirect effects (ecosystem-level) as a measure of propagation of impacts.

The susceptibility of organisms to exposure from chemical stress largely depends on the mobility of the organisms, their home-range in relation to the exposed area, and their capability to actively avoid exposure.

Intrinsic sensitivity is related to the effect of chemicals at the individual level and can be explained by the toxicokinetics (TK) and toxicodynamics (TD) of a substance in the exposed organisms (Nyman et al. 2014, Rubach et al. 2012). TK are determined by traits such as surface/volume ratio, breathing mode, lipid content, dietary habits and rate of metabolic degradation. Differences in metabolic rates have been suggested as a key factor determining species sensitivity (Baas and Kooijman 2015) but data are often unavailable or difficult to generate. TD, in contrast, depend on the chemical mode(s) of action, on cellular-scale damage-repair mechanisms and on the adverse outcome pathway from cellular to organism scale. In general, greater interspecific variations in TD are expected for specifically acting chemicals, such as biocides or pharmaceuticals, than for baseline toxicants, such as the majority of home and personal care ingredients (Rubach et al., 2011). Unfortunately, the information available is often insufficient or inconclusive for determining the most important toxicity mechanism(s). Many biocides used in home and personal care products affect multiple target sites and metabolic pathways in microbial cells, which may reflect in multiple toxicity mechanisms in non-target organisms (e.g. Dann and Hontela 2011). In other cases, toxicity mechanisms of high concern, such as endocrine effects have been observed in the lab (Kunz et al. 2006), but it remains unclear whether these represent the major toxicity mechanism at environmentally relevant concentrations for chemicals suspected of endocrine effects.

Population sustainability is determined by demographic and reproductive traits including voltinism, dispersal capacity, swimming mode, drifting ability, and the presence of emergent life

stages (Beketov et al. 2008; Van den Brink et al. 1996; Galic et al. 2012 and 2014; Rico and Van den Brink 2015). Traits can be used to assess the vulnerability of the different species, populations and communities to chemical exposure. Sensitivity-related traits can be used to evaluate the relative sensitivity of aquatic organisms to chemical exposure. For example, Baird and Van den Brink (2007) and more recently Rubach et al. (2012) and Rico and Van den Brink (2015) identified particular correlations between some traits and the empirical sensitivity of aquatic organisms. In the study by Rico and Van den Brink (2015), regression models were established that allow prediction of the relative sensitivity of aquatic invertebrates to some specific insecticidal modes-of-action. Similar correlations could be established for down-the-drain chemicals with known mode of action allowing the ranking of species according to their expected sensitivity. In a similar way, traits could be used to rank the species according to their recovery potential in time and space. The statistical significance and the uncertainty associated to such correlations will depend on the quantity and quality of available toxicity data. Several examples exist in the literature that deal with the identification of vulnerable aquatic taxa impacted by pesticide exposure in surface waters (e.g. Ibrahim et al. 2014; Gergs et al. 2011; Rico and Van den Brink 2015); Comparable examples for species inhabiting larger lotic systems impacted by down-the drain chemicals remains to be developed. For this, it is important to take into consideration the exposure dynamics resulting from semi-continuous point-source emission of down-the-drain chemicals in surface waters. Besides intrinsic sensitivity, traits related to mobility and habitat range of different taxonomic groups will influence the effects on population abundances. Three conceptual spatial scenarios can be outlined for lotic systems (Figure 2). Small planktonic organisms (Figure 2a), for instance, are likely to be influenced by the occurrence of drift and so effects may be seen further downstream, depending on their

population-level recovery traits (e.g. reproductive behaviour). The population abundance of benthic organisms such as rooted macrophytes or benthic invertebrates downstream of effluent discharge points is likely to be characterized by their dispersal and reproductive behaviour (Figure 2b). The recolonization of areas in which chemical exposure exceeds sensitivity thresholds thus causing direct toxic effects will only be achieved if the species is able to adapt physiologically or genetically to the chemical. In contrast, fish species (Figure 2c), which usually have a larger home-range than the area in which exposure results in toxic effects, may hardly show abundance declines in specific areas, and will require a larger-scale spatial evaluation to observe population declines. Traits such as active avoidance, migration, and swimming behaviour will influence their distribution, in relation to hotspots of chemical exposure or other stress factors.

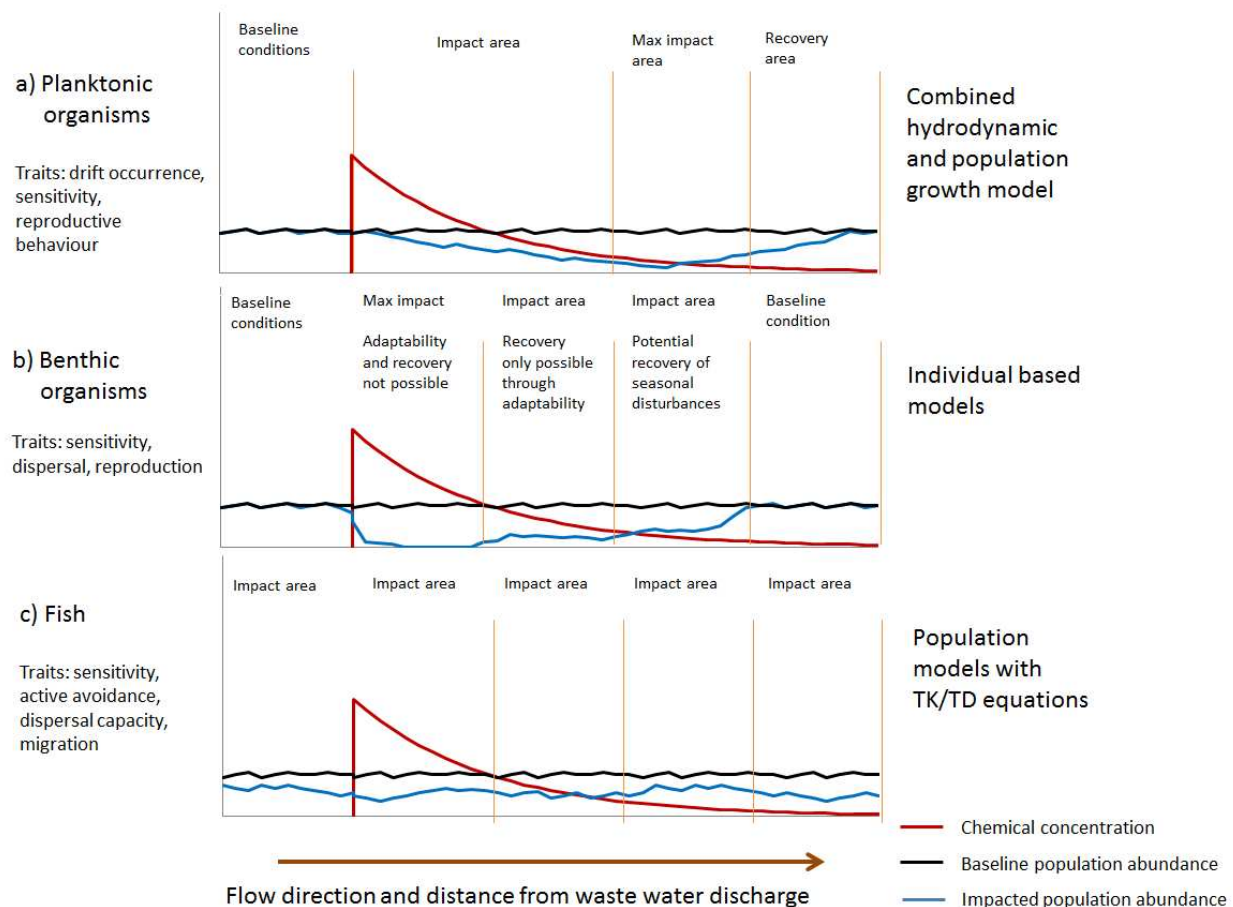


Figure 2. Conceptual spatial illustration of population-level toxic effects expected after point-source chemical discharges for different taxonomic groups. The main traits characterising vulnerability potential (left) and the most suitable modelling approach for assessing the ecotoxicological risks (right) are presented.

Construction of food-web scenarios

Food web scenarios can be constructed from available quantitative and/or qualitative biomonitoring data and relying basic fundamental constraints related to the conservation of (bio)mass and energy within and across biota compartments (e.g. production of one group is enough to support the consumption of its predator). The most important functional groups from

the taxonomic and traits analyses need to be assembled into representative food-web structures so an adequate representation ecosystem-level interactions can be acquired to assess community- and ecosystem-level endpoints. These include interactions affecting internal exposure (e.g. biomagnification) (De Laender et al. 2009 and many others) as well as responses to stress (e.g. competition for resources, predation) (De Hoop et al. 2013, De Laender and Janssen 2013). In addition, the food web structure influences the vulnerability of community assemblages at the ecosystem level (ecosystem vulnerability). From the above considerations of vulnerability, it is clear that a daunting number of variables potentially influence ecological effects and therefore risk. Unfortunately, only a limited amount of experimental data are available to evaluate if and how the variables making up the environmental scenario actually cause variation among ecosystem-level responses to chemicals. To overcome this data gap, De Laender et al. (2015) used mechanistic models to theoretically explore the influence of various ecological variables on the response of ecosystems to different types of chemicals. In these simulations ecosystem-level effects were larger in mesotrophic systems than in oligotrophic systems, suggesting trophic state as an important variable. Regardless of trophic state, interaction strength (quantified using grazing rates) was suggested as a more important driver for the size and recovery from direct and indirect effects than dispersal rate. Such theoretical exercises stress the need to focus on vulnerable ecosystem scenarios to feed on-going developments of ecological modelling for risk assessment (De Laender et al. 2015).

The selection of the spatial scale is often a critical step in constructing a food web for a certain ecosystem, particularly for open, lotic systems. In doing so, the species with the largest lifetime spatial range will define the scale of the whole ecosystem to be considered, because other elements which have smaller spatial ranges will re-occur within the large system. For example,

periphyton or macrophytes influence and are influenced by the surrounding environment at a very limited scale at the individual level, but populations colonise wider areas, so it is possible to integrate them into a fish-dominated ecosystem also in a spatially-explicit sense.

4. SCENARIO-BASED ECOLOGICAL MODELS FOR RISK ASSESMENT

Environmental scenarios developed at different scales and levels of resolution (Figure 1) can be applied in a tiered risk assessment framework according to the level of confidence required at a given tier. The degree of integration between exposure and effect assessment is expected to be most refined at the highest tier since the matching of the abiotic parameter values and the spatial-temporal scales is maximized. The spatial and temporal integration of exposure and effects models is one of the key challenges in a risk assessment framework. Spatial resolution in exposure and effects assessments can be fully integrated only if exposure and effect models are spatially explicit at a consistent scale. This may only be feasible in specific high tier assessments. In contrast, the implementation of temporally explicit modelled exposure data into the TK component of ecological models is relatively straightforward because most TK models are designed to simulate dynamic exposure.

Below we outline potential approaches to introduce ecological realism and greater mechanistic understanding in a tiered framework for prospective risk assessment of down-the-drain chemicals. Ecological effect models can be developed for identified vulnerable species (Figure 1). Different types of effect models, ranging from organism- to ecosystem-level may be used to assess ecologically relevant endpoints according to the SPGs derived to protect structural integrity (e.g. biodiversity) or specific ecosystem services.

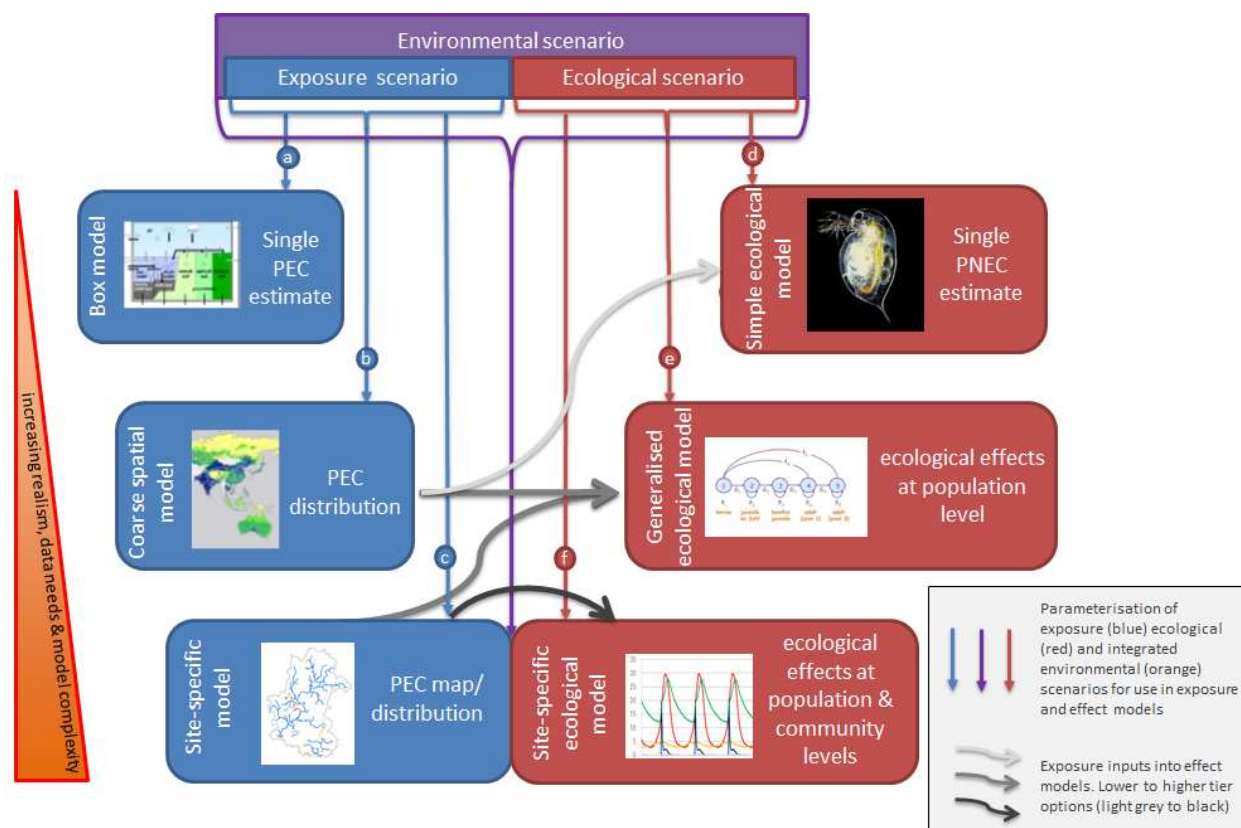


Figure 3. Conceptual framework illustrating options to combine scenario-based exposure and ecological effects models. Box models representing simplistic scenarios (Figure 3, a) can be used in combination with simple effect assessments, i.e. PNECs derived from standard single-species laboratory tests (Figure 3, d) for screening assessment. Large scale to regional exposure scenarios (Figure 3, b) modelled by coarse spatial models can be used to identify chemical exposure hotspots and to generate exposure and risk maps. Exposure data from coarse exposure models (Figure 3, b) can be used as inputs for individual- and/or population-level models (Figure 3, e). Site-specific (sub)catchment-scale exposure scenarios (Figure 3, c) can be then parameterised for selected exposure “hotspots”. Site-specific exposure data can feed into individual- and/or population-level scenarios for focal taxa (Figure 3, e) or for vulnerable ecosystems scenarios (Figure 3, f).

4.1 Linking exposure to individual level effects

A requisite for the accurate integration of exposure and effect assessments is the use of consistent exposure data (i.e. total, bioaccessible or bioavailable concentrations). The bioavailable exposure concentration depends on by environmental factors (e.g. sorption to organic matter), which is why the free aqueous concentration is more representative of the exposure experienced by aquatic organisms and, therefore, the most appropriate exposure metric for linking exposure and effects. However, it is not the external concentration that causes the effect, but rather the concentration at the target site. Therefore, using internal dose as a metric can begin to account for the species sensitivity differences caused by toxicokinetics (Escher and Hermens 2004, Hendriks et al. 2005, Nyman et al. 2014). Toxicokinetic-toxicodynamic models can explicitly separate TK from TD processes (Ashauer et al. 2015). Thus, it is possible to model the influence of physical-chemical properties, some species traits (Rubach et al. 2012, Buchwalter et al. 2008, Poteat and Buchwalter 2014) and environmental factors (Ruotsalainen et al. 2010) on toxicokinetics as well as the influence of toxicity pathways (Lalone et al. 2013, Gunnarson et al. 2008), species traits (Rubach et al. 2012) and environmental factors (Heugens et al. 2003) on toxicodynamics (Ashauer et al. 2015, Rubach et al. 2011, Jager 2013). In some cases a single parameter, such as temperature, can influence both TK, by changing uptake, elimination and biotransformation rates (Heugens et al. 2003, Harwood et al. 2009, Buchwalter et al. 2003), as well as TD by changing physiology and intrinsic sensitivity (Harwood et al. 2009).

The physiological and ecological parameterisation of effect models can, to a large extent, be based on species traits information or on collections of model parameters for specific modelling approaches, e.g. the add-my-pet database for dynamic energy budget (DEB) models (http://www.bio.vu.nl/thb/deb/deblab/add_my_pet/; Lika et al. 2011). Such parameterisations

will set the baseline for any selected taxonomic aggregation. In contrast, parameterisation of chemical effects requires significant experimental efforts. In some cases, detailed toxicity test results for vulnerable species will be available and can be used for parameterisation of the TD component of effect models, but such cases will probably be more the exception than the rule. Chronic experimental tests will be required, ideally using most vulnerable species, and need to include measurements of reproduction and growth over time (Lika et al. 2011).

Ecological relevance of environmental risk assessments can be increased by integrating chemical stress with other environmental and anthropogenic stress variables. Although the impact of environmental factors such as temperature, food availability, competition and predation on organisms' responses to chemical stress has been observed experimentally (e.g. Heugens et al. 2003, Stampfli et al. 2011, Del Arco et al. 2015), the ability of ecological models to predict interactions between such factors and chemical stress remains largely untested. The integration of environmental and chemical stressors requires models at the organism-level because stressors impact survival, growth, and reproduction at this scale. Environmental stress, such as starvation, has been integrated with toxic effects on survival in a straightforward model by treating in a similar way environmental and chemical stress (Nyman et al. 2013). Integrating environmental stressors with chemical effects on sub-lethal endpoints (e.g. growth, reproduction) is more challenging because growth and reproduction are interrelated via an organisms' energy allocation (Jager 2013, Sousa et al. 2010). However DEB models offer a platform to simulate sub-lethal, organism level toxicity and integrate environmental stressors because the modification of toxic effects on growth and reproduction by environmental factors will also act via changes to the organisms' energy allocation (Jager 2013). For example, in a DEB modelling framework food limitation can be modelled by lower energy intake, and competition or

physiological stress by higher energy requirements for maintenance (e.g. due to wider foraging ranges) on the organism level. Future research needs to define the relationships between the effect model parameters and the main environmental factors that influence survival, growth and reproduction of different species. Temperature, food availability as well as water quality stressors associated with domestic wastewater (e.g. oxygen deficit, ammonia) are among the most sensitive parameters in DEB models and need to be included in forthcoming research. Of course other, non-energy related interactions are also conceivable (e.g. photosensitivity), which would require additional modelling.

4.2 Population level effects models

Population models can be applied at the higher tiers of the proposed framework (Figure 3). They can link individual-level effects to relevant processes at the population level such as reproduction, density dependent regulation mechanisms, or dispersal, which determine population dynamics. The consideration of sub-lethal effects, in particular, requires an appropriate integration of individual-level models into population-level models to capture long term effects. Further, population models can function as building blocks to simulate and to analyse species interactions and hence build the interface to community level modelling. Population models for combinations of species groups (defined by key traits) and endpoints need to be developed based on the existing portfolio of population modelling approaches. The physiological/ecological parameterisation of population models can to a large extent be based on collections of species traits that exist for fish, benthic invertebrates (e.g. Poff et al. 2006; Usseglio-Polatera et al. 2000) and aquatic macrophytes.

For fish, many relevant traits such as avoidance, dispersal capacity and migration have an explicit spatial dimension (Figure 2). Therefore, population models need to integrate individual level sub-lethal effects with population level processes in a spatially explicit environment. The model time frame needs to be sufficiently long to cover multiple life cycles, which for fish may require simulation periods of several years. Population-level models for fish require individual-level exposure history data in a spatially explicit context as input of TK/TD model components, which link resulting sub-lethal effects, e.g. on body size, to the relevant population-level processes, i.e. reproduction, energy demands, etc. (Beaudouin et al 2015) .

In the case of benthic invertebrates and rooted macrophytes, which disperse over smaller spatial scales compared to fish and generally occur in higher numbers, individual-based models (IBMs) or compartment-based ordinary differential equation models are suitable modelling approaches. IBMs have been combined with TK/TD components (Baveco et al. 2014), including DEB models, which can account for sublethal effects (Martin et al. 2012). Population models still need to account for site-specific exposure whilst including population-level density regulation mechanisms. For example, an IBM population model for the water louse *A. aquaticus* has been integrated with spatially-explicit landscape-level dynamic fate models for pesticides in an agricultural environmental scenario (Focks et al., 2014). Analogous modelling approaches for down-the-drain chemicals may need a different spatial resolution because variability in exposure is probably more significant at larger scales. Exposure data for prioritised catchment-scale environmental scenarios (Figure 3) would inform such requirements.

Planktonic organisms that passively move with the water flow require the integration of population models with appropriate hydrological information (Figure 2). One conceptually

straight forward method is to integrate population-level dynamics with hydrology-based catchment scale fate models with a mass balance approach using ordinary differential equations.

4.3 Community level effects models

Community ecology is concerned with understanding how abiotic variables and interactions between and within species determine coexistence, community composition, and various aspects of biodiversity (Chesson 2000). Two-species individual-based models have been developed to examine the role of species interactions on pesticide effects and subsequent recovery (Viaene et al. 2015). Most communities, however, consist of many more species, especially at lower trophic levels. For example, the site-specific macroinvertebrate species richness in temperate European lotic ecosystems may vary between <10 in small agricultural ditches to >50 in larger rivers (Davies et al. 2008). Recently, a model has been developed to predict community composition and biodiversity along gradients of chemical stress (De Laender et al. 2014b). This approach can be considered a stochastic formulation of an individual-based model (Black and McKane, 2012) and works by calculating the probabilities of reproduction and death per species at each time step, based on the environmental chemical concentration and the inter- and intraspecific variability in sensitivity. The model has been shown to correctly predict algal diversity along herbicide and metal toxicity gradients in lentic systems. Its main advantage is that it only needs a distribution of algal EC₅₀s that represents interspecific variability and an estimation of the long-range passive dispersal rate (the number of immigrants per period of time). A disadvantage is that it does not account for large niche differences between species and that its validity has not been proven for communities other than algae. Overall, this is a pragmatic approach for algae,

considering the high number of algal species and the smaller niche differences compared to heterotrophs.

4.4 Ecosystem level effects models

Ecosystem ecology is concerned with fluxes of matter and energy between functional groups and the abiotic environment, mostly using food web theory to describe the direction and magnitude of these fluxes. Thus, ecosystem-level effect models in chemical risk assessment are used to simulate effects on such fluxes (ecosystem functioning) and on the size of functional groups (ecosystem structure). In general, these models are able (Everaert et al. 2015) to realistically reproduce seasonal fluctuations of biomass and nutrients observed in the field (e.g. Sommer et al. 1986). They are an ideal platform for integrating exposure and ecological scenarios because they can simulate seasonal dynamics of biotic and abiotic variables (e.g. biogeochemical cycles) with which the functional groups interact and on which the exposure of certain chemicals may depend. By integrating chemical stress with general chemical water quality stressors associated with wastewater, such as organic load, nutrients, ammonia or nitrite, ecosystem-level effect models can provide a more realistic representation of the Impact Zone concept, which has been suggested for risk assessment of down-the-drain chemicals in untreated discharge scenarios (Finnegan et al. 2009). Ecosystem-level models are also the best choice for studying indirect chemical effects (Fleege et al. 2003). Modelling indirect effects is most important when transient or local scale effects are acceptable or if indirect effects are greater than direct effects. Ecosystem-level models come in a variety of structural complexity and taxonomic resolution. In their simplest form, they are composed of a limited set of ordinary differential equations that are coupled according to food web interactions and extended with

concentration-response relationships in a non-spatially explicit environment (e.g. De Laender et al. 2008b; De Laender et al. 2015; Everaert et al. 2015). Nutrient dynamics can be either explicitly modelled (e.g. De Laender et al. 2008b) or considered as external forcing functions (e.g. De Laender et al. 2015). One example of such a model, the Aquatox model (Park et al. 2008) is of intermediate complexity and combines (inorganic and organic) nutrient dynamics, food web interactions, chemical fate and more detailed ecotoxicological processes in site-specific integrated environmental scenarios. Recently, Aquatox has been used to simulate potential ecosystem-level effects of two ingredients founds in Home and Personal Care (HPC) products in a lowland river ecosystem (Lombardo et al. 2015). This study showed that indirect effects can be of similar magnitude as direct effects, and can both exacerbate and compensate for direct chemical toxicity. To our knowledge, the highest level of ecosystem model complexity seen to date is currently being developed, where networks of IBMs are constructed that simulate ecosystem dynamics, starting from individual-level processes (De Laender et al. 2014a).

A major challenge to community and ecosystem effect model development and use is calibration (identifying parameter values) and validation (comparing predictions with observations not used during calibration). Because of the level of biological organisation considered, model calibration and validation is cumbersome in practice (but see De Laender et al. 2008a; Sourisseau et al. 2008). Indeed, mesocosm studies will not always be available for a given chemical, let alone cosm studies that encompass ecological responses for different environmental scenarios. An alternative option is to carry out lab-scale studies for a selection of stress scenarios that examine how processes key to community composition or ecosystem functioning (e.g. competition, predation) combine with chemicals in affecting simplified study

systems consisting of few species (Viaene et al. 2015; Liess and Foit, 2010; De Hoop et al. 2013).

4.5 Uncertainty analysis and probabilistic approaches to decision making

The technical challenge of incorporating the seemingly overwhelming complexity of stress ecology into a pragmatic risk assessment framework calls for a holistic consideration of uncertainty. Uncertainty, broadly defined as the combination of epistemic uncertainty and variability, needs to be assessed at different levels, from scenarios (e.g. variability and representativeness of scenarios) to model and parameters uncertainty.

Quantitative sensitivity and uncertainty analysis of model input data and parameters has been addressed in exposure models used in regulatory frameworks (Matthies et al. 2004, Hollander et al. 2009), but far less attention has been paid to higher levels of uncertainty, especially those associated with the definition of the scenario (Hollander et al. 2009) or with the mathematical representation of that scenario (model uncertainty). We envision the use of iterative model simulation at increasing resolution combined with sensitivity and uncertainty analysis to refine sensitive parameters in prioritised scenarios. Global to catchment scale exposure scenarios will be compared and evaluated for their ability to identify exposure hotspots and for their accuracy in predicting measured concentrations. Specific enhancements such as the refined parameterisation of compartment phases (e.g. the distinction between dissolved and suspended organic matter), transport processes (e.g. dynamic solids transport) or the addition of environmental processes not usually included in multimedia fate models (e.g. wastewater reuse, irrigation) could be implemented at higher tiers, if statistically relevant.

Consideration of scenario and model uncertainty in ecological effect assessments is an essential part of the development of ecological scenarios. The validity of the ecological component of environmental scenarios needs to be evaluated based on the uncertainty associated with the identification of most sensitive taxa/traits and of worst case ecosystem conditions. Admittedly, our current ability to predict population vulnerability and intrinsic sensitivity in the first place is a crucial source of uncertainty. The choice of the level of detail in individual to ecosystem-level processes together with the selected spatial scale define the model complexity as well as computational demands. It is obvious that not all aspects mentioned here can be maximised at the same time. Models of varying complexity should be compared by balancing accuracy in predictions with uncertainty introduced by additional parameters to identify the optimal level of complexity (De Laender et al. 2014; Baveco et al., 2014). Finding the optimal number of processes driving the dynamics of species or functional groups is most challenging when developing models describing the community level. This is because the objective of such a model would be to simulate potential effects on multiple species, each having a distinct environmental response, sensitivity, and specific interactions with the rest of the community. Clearly, not all this complexity can be accounted for because model implementation would no longer be technically feasible, results difficult to interpret and parameters poorly identifiable. In practice, model developers will have to decide what mechanisms to include in community models and where to simplify. Methods such as approximate Bayesian computation are excellent tools to identify what mechanisms contribute most to observed patterns and thus to optimize model complexity (Hartig et al. 2011). Finally, we envision that models should be run through an ecological sensitivity analysis using realistic ranges of physiological parameters and environmental stress variables for a given scenario to identify an optimal model complexity and

to refine sensitive parameters (Figure 4). Once established, a probabilistic parameterisation can be implemented to account for environmental variability and for uncertainty in that scenario. Defining the values of environmental parameters under baseline and stress scenarios is part of the development of environmental scenarios. In organism level effect models this can be achieved by reviewing existing knowledge or using model simulations under different stress scenarios (e.g. in a DEB model environment) to derive ranges of physiological parameters. A probabilistic, scenario-based approach as suggested here lends itself to the creation of effect – prevalence plots that can serve as a basis for risk assessment. Figure 4 illustrates an example of an effect-prevalence plot for an organism-level endpoint (e.g. reduced number of offspring or delayed time to maturity) in a given hypothetical environmental scenario. The lines in such plots can be generated from the Monte-Carlo analysis of the coupled models, representing the different environmental variables and stress scenarios. The same concept can be applied to address population-level and community level endpoints (e.g. reduction in population abundance or reduction in biodiversity indicators). For any given exposure or ecological scenario, an effect-prevalence plot can be generated to form the evidence base for decision making.

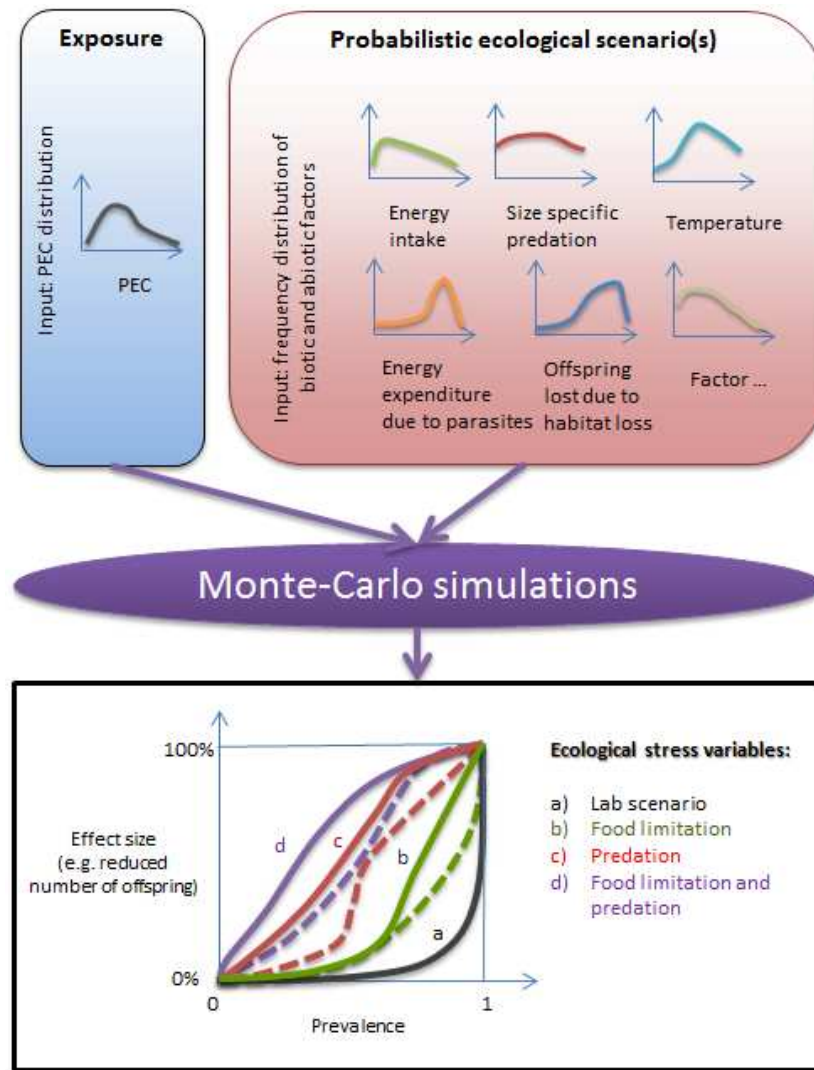


Figure 4. Application of a probabilistic risk assessment for a generalised environmental scenario. Example of individual-level effect-prevalence plots for a given species in unexposed (dashed line) and exposed (full line) scenarios introducing ecological stress variables. The x-axis can represent different types of effect, (e.g. reduction in offspring).

5. SUMMARY OF RESEARCH PRIORITIES

Our analysis departs from the awareness that embracing ecological realism and spatial variation on community structure and function in future risk assessment requires a new

framework rather than incremental changes to the existing framework. We believe that a scenario-based approach that integrates spatially explicit exposure models with ecological effect models for vulnerable taxa is needed to address the challenge. This is a long-term proposition. Examples cited in this paper demonstrate technical feasibility of advanced model-based approaches to refine exposure and ecological effects assessment. However, challenges remain in application to prospective regulatory risk assessment which require significant research efforts. We propose the following research priorities to enable the implementation of a scenario-based ecological risk assessment modelling framework for down-the-drain chemicals:

- Develop a spatially and possibly temporally explicit exposure modelling framework that allows tiered exposure assessment of down-the-drain chemicals from global to catchment scale. Evaluation against monitoring data combined with sensitivity and uncertainty analysis will inform refinement needs for simulations at higher resolution.
- Collect taxonomic and traits data to extract representative ecological scenarios starting from well-studied river catchments exposed to discharges of wastewater effluents. The combination of biological datasets, such as those collected as part of the WFD program in Europe, with available traits datasets offers an opportunity in this direction.
- Implement a new paradigm in toxicity testing based on a tiered risk assessment that moves from standard test species and protocols towards a targeted approach focused on long-term effects on most sensitive species/traits, including non-standard species. Tests need to be designed to facilitate the development, parameterisation and the evaluation of effect models and to enable the consideration of key environmental variables and stressors. Among these, food availability, temperature as well as wastewater-related stressors such as oxygen depletion and ammonia are most relevant to down-the-drain chemicals.

- Develop effect models for focal species and compare modelling options to identify the optimal complexity for different ecological scenarios. The optimal model structure balances i) taxonomic resolution with generalisations or read-across options and ii) mechanistic detail with model complexity and associated data requirements.
- Develop proof of principle examples of integrated exposure and effect model-based assessments that use ecologically relevant effect endpoints as a basis for decision making in chemical risk assessment.

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References

- [EFSA] European Food Safety Authority. 2014. Scientific Opinion on good modelling practice in the context of mechanistic effect models for risk assessment of plant protection products. *EFSA Journal* 12(3): 3589-3592.
- [EEA] European Environment Agency. 2015. European Freshwater Ecosystem Assessment: Cross-walk Between the Water Framework Directive and Habitats Directive Types, Status and Pressures. Cited 2015-10-30. Available from: <https://circabc.europa.eu/w/browse/f94f35e6-5edc-4426-baf3-0a306bb7c68a>.
- Alexander AC, Luis AT, Culp JM, Baird DJ, Cessna AJ. 2013. Can nutrients mask community responses to insecticide mixtures? *Ecotoxicology* 22:1085–1100.
- Aronson D, Weeks J, Meylan B, Guiney DP, Howard HP. 2012. Environmental release, environmental concentrations, and ecological risk of N,N-diethyl-m-toluamide (DEET). *Int Environ Assess Manag* 8: 135-166.
- Ashauer R, O'Connor I, Hintermeister A, Escher BI. 2015. Death Dilemma and Organism Recovery in Ecotoxicology. *Environ Sci Technol* 49: 10136–10146.
- Augusiak J, Van den Brink PJ, Grimm V. 2014. Merging validation and evaluation of ecological models to ‘evaluation’: a review of terminology and a practical approach. *Ecol Modelling* 280: 117-128.
- Baas J, Kooijman SALM. 2015. Sensitivity of animals to chemical compounds links to metabolic rate. *Ecotoxicology* 24: 657-663.
- Baird DJ, Van den Brink PJ. 2007. Using biological traits to predict species sensitivity to toxic substances. *Ecotoxicol Environ Saf* 67: 296–301.

Baird DJ, Van den Brink PJ, Chariton AA, Dafforn KA, Johnston EL. 2015. New diagnostics for multiply stressed marine and freshwater ecosystems: integrating models, ecoinformatics and big data. *Mar Freshwater Res.* (accepted)

Baveco JMH, Norman S, Roessink I, Galic N, Van Den Brink PJ. 2014. Comparing population recovery after insecticide exposure for four aquatic invertebrate species using models of different complexity. *Environ Toxicol Chem* 33: 1517-1528.

Beaudouin R, Goussen B, Piccini B, Augustine S, Devillers J, Brion F, Péry ARR. 2015. An individual-based model of zebrafish population dynamics accounting for energy dynamics. *PLoS ONE* 10(5).

Beketov MA, Schäfer RB, Marwitz A, Paschke A, Liess M. 2008. Long-term stream invertebrate community alterations induced by the insecticide thiacloprid: Effect concentrations and recovery dynamics. *Sci Tot Environ* 405: 96–108.

Black AJ, McKane AJ. 2012. Stochastic formulation of ecological models and their applications. *Trends Ecol Evol* 27: 337–345.

Borja A, Josefson AB, Miles A, Muxika I, Osgard F, Phillips G, Germán Rodríguez J, Rygg B. 2007. An approach to the intercalibration of benthic ecological status assessment in the North Atlantic ecoregion, according to the European Water Framework Directive. *Mar Pollut Bull* 55: 42–52.

Buchwalter DB, Cain DJ, Martin CA, Xie L, Luoma SN, Garland Jr T. 2008. Aquatic insect ecophysiological traits reveal phylogenetically based differences in dissolved cadmium susceptibility. *Proc. Natl. Acad. Sci. U. S. A.* 105: 8321-8326.

Buchwalter DB, Jenkins JJ, Curtis LL. 2003. Temperature influences on water permeability and chlorpyrifos uptake in aquatic insects with differing respiratory strategies. *Environ. Toxicol. Chem.* 22: 2806-2812.

Chesson P. 2000. Mechanisms of maintenance of species diversity. *Annu Rev Ecol Syst* 31: 343–366.

Dale AL, Lowry GV, Casman E. 2015. Stream dynamic and chemical transformation control the environmental fate of silver and zinc oxide nanoparticles in a watershed-scale model. *Environ Sci Technol* 49: 7285-7293.

Davies B, Biggs J, Williams P, Withfield M, Nicolet P, Seac D, Bray S, Maund S. 2008. Comparative biodiversity of aquatic habitats in the European agricultural landscape. *Agric Ecosyst Environ* 125: 1-8.

Dann AB, Hontela A. 2011. Triclosan: environmental exposure, toxicity and mechanisms of action. *J Appl Toxicol* 31: 285-311.

De Hoop L, De Troch M, Hendriks AJ, De Laender F. 2013. Modeling toxic stress by atrazine in a marine consumer-resource system. *Environ Toxicol Chem* 32: 1088–95.

De Laender F, De Schamphelaere KAC, Vanrolleghem PA, Janssen CR. 2008a. Comparison of different toxic effect sub-models in ecosystem modelling used for ecological effect assessments and water quality standard setting. *Ecotoxicol Environ Saf* 69: 13-23.

De Laender F, De Schamphelaere KAC, Vanrolleghem PA, Janssen CR. 2008b. Validation of an ecosystem modelling approach as a tool for ecological effect assessments. *Chemosphere* 71: 529-545

De Laender F, Janssen CR. 2013. Brief communication: the ecosystem perspective in ecotoxicology as a way forward for the ecological risk assessment of chemicals. *Int Environ Assess Manag* 9: e34-e38.

De Laender F, Melian CJ, Bindler R, Van den Brink PJ, Daam M, Roussel H, Juselius J, Verschuren D, Janssen CR. 2014b. The contribution of intra- and interspecific tolerance variability to biodiversity changes along toxicity gradients. *Ecol Lett* 17: 72-81.

De Laender F, Van Oevelen D, Middelburg J, Soetaert K. 2009. Incorporation of ecological data and associated uncertainty in bioaccumulation modelling. *Environ Sci Technol* 43: 2620-2626

De Laender F, Morselli M, Baveco H, Van den Brink PJ, Di Guardo A. 2015. Theoretically exploring direct and indirect chemical effects across ecological and exposure scenarios using mechanistic fate and effects modelling. *Environ Int* 74: 181-190.

De Laender F, Van den Brink PJ, Janssen CR, Di Guardo A. 2014a. The ChimERA project: Coupling mechanistic exposure and effect models into an integrated platform for ecological risk assessment. *Env Sci Pollut Res* 21: 6263-6267.

Del Arco AI, Rico A, Van den Brink PJ. 2015. Effects of intra- and interspecific competition on the sensitivity of *Daphnia magna* populations to the fungicide carbendazim. *Ecotoxicology* 24: 1362–1371.

Escher BI, Hermens JLM. 2004. Internal exposure: Linking bioavailability to effects. *Environ Sci Technol* 38: 455A-462A.

Everaert G, De Laender F, Goethals PL, Janssen CR. 2015. Relative contribution of persistent organic pollutants to marine phytoplankton biomass dynamics in the North Sea and the Kattegat. *Chemosphere* 134:76-83.

Finnegan CJ, van Egmond RA, Price OR, Whelan MJ. 2009. Continuous-flow laboratory simulation of stream water quality changes downstream of an untreated wastewater discharge. *Water Res* 43: 1993-2001.

Fleegeer JW, Carman KR, Nisbet RM. 2003. Indirect effects of contaminants in aquatic ecosystems. *Sci Tot Environ* 317: 207–233.

Focks A, ter Horst M, van den Berg E, Baveco H, van den Brink PJ. 2014. Integrating chemical fate and population-level effect models for pesticides at landscape scale: New options for risk assessment. *Ecol Modelling* 280: 102-116.

Forbes VE, Calow P, Grimm V, Hayashi TI, Jager T, Katholm A, Palmqvist A, Pastorok R, Salvito D, Sibly R, Spromberg J, Stark J, Stillman RA. 2011. Adding value to ecological risk assessment with population modeling. *Hum Ecol Risk Assess* 17: 287-299.

Forum for the Coordination of Pesticide Fate Models and Their Use. 2001. FOCUS surface water scenarios in the EU evaluation process under 91/414/EEC. Report, EC Document Reference SANCO/4802/2001-rev.1. FOCUS Working Group on Surface Water Scenarios, Brussels, Belgium.

Gabsi F, Schäffer A, Preuss TG. 2014. Predicting the sensitivity of populations from individual exposure to chemicals: The role of ecological interactions. *Environ Toxicol Chem* 33:1449–57.

Galic N, Hommen U, Baveco HJM, van den Brink PJ. 2010. Potential application of population models in the European ecological risk assessment of chemicals II: review of models and their potential to address environmental protection aims. *Int Environ Assess Manag* 6: 338-360.

Galic N, Baveco H, Hengeveld GM, Thorbek P, Bruns E, Van den Brink PJ. 2012. Simulating population recovery of an aquatic isopod: effects of timing of stress and landscape structure. *Environ Pollut* 163: 91-99.

- Galic N, Ashauer R, Baveco H, Nyman A-M, Barsi A, Thorbek P, Bruns E, Van den Brink PJ. 2014. Modelling the contribution of toxicokinetic and toxicodynamic processes to the recovery of *Gammarus pulex* populations after exposure to pesticides. *Environ Toxicol Chem* 33: 1476–1488.
- Gergs A, Classen S, Hommen U. 2011. Identification of realistic worst case aquatic macroinvertebrate species for prospective risk assessment using the trait concept. *Environ Sci Pollut Res* 18:1316–1323.
- Gergs A, Classen S, Strauss T, Ottermanns R, Brock TCM, Ratte H-T, Hommen U, Preuss TG. 2016. Ecological recovery potential of freshwater organisms – consequences for environmental risk assessment of chemicals. *Rev Environ Contam T* 236: 259-294.
- Gunnarsson L, Jauhiainen A, Kristiansson E, Nerman O, Larsson DGJ. 2008. Evolutionary conservation of human drug targets in organisms used for environmental risk assessments. *Environ Sci Technol* 42: 5807-5813.
- Grill G, Khan U, Lehner B, Nicell J, Ariwi J. 2016. Risk assessment of down-the-drain chemicals at large spatial scales: model development and application to contaminants originating from urban areas in the Saint Lawrence river basin. *Sci Tot Environ* 541: 825-838.
- Hartig F, Calabrese JM, Reineking B, Wiegand T, Huth A. 2011. Statistical inference for stochastic simulation models--theory and application. *Ecol Lett* 14: 816–827.
- Harwood AD, You J, Lydy MJ. 2009. Temperature as a toxicity identification evaluation tool for pyrethroid insecticides: Toxicokinetic confirmation. *Environ. Toxicol. Chem.* 28: 1051-1058.
- Helmes R, Huijbregts MAJ, Henderson AD, Jolliet O. 2012. Spatially explicit fate factors of freshwater phosphorous emissions at the global scale. *Int J LCA* 17: 646-654.

Hendriks AJ, Traas TP, Huijbregts MAJ. 2005. Critical body residues linked to octanol-water partitioning, organism composition, and LC50 QSARs: Meta-analysis and model. *Environ Sci Technol* 39: 3226-3236.

Heugens EHW, Jager T, Creighton R, Kraak MHS, Hendriks AJ, Van Straalen NM, Admiraal W. 2003. Temperature-dependent effects of cadmium on *Daphnia magna*: Accumulation versus sensitivity. *Environ Sci Technol* 37: 2145-2151.

Heugens EHW, Tokkie LTB, Kraak MHS, Hendriks AJ, Van Straalen NM, Admiraal W. 2006. Population growth of *Daphnia magna* under multiple stress conditions: joint effects of temperature, food and cadmium. *Environ Toxicol Chem* 25: 1399-1407.

Hodges JE, Holmes CM, Vamshi R, Mao D, Price OR. 2012. Estimating chemical emissions from home and personal care products in China. *Environ Pollut* 165: 199-207.

Hollander A, Pistocchi A, Huijbregts MAJ, Ragas AMJ, Van De Meent D. 2009. Substance or space? The relative importance of substance properties and environmental characteristics in modeling the fate of chemicals in Europe. *Environ Toxicol Chem* 28: 44-51.

Hommen U, Baveco HJM, Galic N, van den Brink P.J. 2010. Potential application of population models in the European ecological risk assessment of chemicals I: review of protection goals in EU directives and regulations. *Int Environ Assess Manag* 6: 325-337.

Humbert S, Manneh R, Shaked S, Horvath A, Deschênes L, Jolliet O, Margni M. 2009. Assessing regional intake fractions and human damage factors in North America. *Sci Tot Environ* 407: 4812-4820.

Ibrahim L, Preuss TG, Schaeffer A, Hommen U. 2014. A contribution to the identification of representative vulnerable fish species for pesticide risk assessment in Europe - A comparison of population resilience using matrix models. *Ecol Model* 280: 65-75.

Jager T. 2013. Making sense of chemical stress. Cited: 2015-10-30. Available from:

<http://www.debttox.info/book.php>.

Kearney M., Porter W. 2009. Mechanistic niche modelling: combining physiological and spatial data to predict species' ranges. *Ecol Let* 12: 334-350.

Kearney M, Simpson SJ, Raubnheimer D, Helmuth B. 2010. Modelling the ecological niche from functional traits. *Phil Tr B* 365: 3469-3483.

Kehrein N, Berlekamp J, Klasmeier J. 2015. Modeling the fate of down-the-drain chemicals in whole watersheds: New version of the GREAT-ER software. *Environ Mod Softw* 64: 1-8.

Kounina A, Margni M, Shaked S, Bulle C, Jolliet O, 2014. Spatial analysis of toxic emissions in LCA: a sub-continental nested USEtox model with freshwater archetypes. *Environ Int* 69: 67–89.

Kunz PY, Galicia HF, Fent K. 2006. Comparison of in vitro and in vivo estrogenic activity of UV filters in fish. *Toxicol Sci* 90: 349-361.

Lalone CA, Villeneuve DL, Burgoon LD, Russom CL, Helgen HW, Berninger JP, Tietge JE, Severson MN, Cavallin JE, Ankley GT. 2013. Molecular target sequence similarity as a basis for species extrapolation to assess the ecological risk of chemicals with known modes of action. *Aquat Toxicol* 144-145: 141-154.

Lehner B, Grill G. 2013. Global river hydrography and network routing: Baseline data and new approaches to study the world's large river systems. *Hydrol Process* 27: 2171-2186.

Liess M, Foit K. 2010. Intraspecific competition delays recovery of population structure. *Aquatic Toxicol* 97: 15-22.

Lika,K, Kearney MR, Freitas V, van der Veer HW, van der Meer J, Wijsman JWM, Pecquerie L, Kooijman, SALM. 2011. The “covariation method” for estimating the parameters of the standard dynamic energy budget model I: Philosophy and approach. *J Sea Res* 66: 270-277.

- Lombardo A, Franco A, Pivato A, Barausse A. 2015. Food web modelling of a river ecosystem for risk assessment of down-the-drain chemicals. *Sci Tot Environ* 508: 214-227.
- Martin BT, Zimmer EI, Grimm V, Jager T. 2012. Dynamic Energy Budget theory meets individual-based modelling: A generic and accessible implementation. *Method Ecol Evol* 3: 445-449.
- Matthies M, Berding V, Beyer A. 2004. Probabilistic uncertainty analysis of the European Union System for the Evaluation of Substances multimedia regional distribution. *Environ Toxicol Chem* 23: 2494-2502.
- Morselli M, Semplice M, De Laender F, Van den Brink PJ, Di Guardo A. 2015. Importance of environmental and biomass dynamics in predicting chemical exposure in ecological risk assessment. *Sci Tot Environ* 526: 338-345.
- Nienstedt KM, Brock T, v Wensem J, Montforts M, Hart A, Aagaard A, et al. 2012. Development of a framework based on an ecosystem services approach for deriving specific protection goals for environmental risk assessment of pesticides. *Sci Tot Environ* 415: 31-38.
- Nyman AM, Hintermeister A, Schirmer K, Ashauer R. 2013. The insecticide imidacloprid causes mortality of the freshwater amphipod *Gammarus pulex* by interfering with feeding behavior. *PLoS ONE* 8: e62472.
- Nyman AM, Schirmer K, Ashauer R. 2014. Importance of Toxicokinetics for Interspecies Variation in Sensitivity to Chemicals. *Environ Sci Technol* 48: 5946-5954.
- Park RA, Clough JS, Coombs Wellman M. 2008. AQUATOX: Modelling environmental fate and ecological effects in aquatic ecosystems. *Ecol Model* 213:1-15.

- Poff NL, Olden JD, Vieira NKM, Finn DS, Simmons MP, Kondratieff BC. 2006. Functional trait niches of North American lotic insects: traits-based ecological applications in light of phylogenetic relationships. *J North Am Benthol Soc* 25:730–775.
- Poteat MD, Buchwalter DB. 2014. Phylogeny and Size Differentially Influence Dissolved Cd and Zn Bioaccumulation Parameters among Closely Related Aquatic Insects. *Environ Sci Technol* 48: 5274-5281.
- Price OR, Munday DK, Whelan MJ, Morris G, Young AR. 2009. Data requirements of GREAT-ER: Modelling and validation using LAS in four UK catchments. *Environ Pollut* 157: 2610-2616.
- Price OR, Thorbek P. 2014. In response: Challenges and opportunities for landscape ecotoxicology and spatially explicit risk assessment – an industry perspective. *Environ Toxicol Chem* 33: 1194-1196.
- Rico A, Van den Brink PJ, Gylstra R, Focks A, Brock TCM. 2015. Developing ecological scenarios for the prospective aquatic risk assessment of pesticides. *Int Environ Assess Manag* (in press) DOI: 10.1002/ieam.1718.
- Rico A, Van den Brink PJ. 2015. Evaluating aquatic invertebrate vulnerability to insecticides based on intrinsic sensitivity, biological traits and toxic mode of action. *Environ Toxicol Chem* 34: 1907-1917.
- Rubach MN, Ashauer R, Buchwalter DB, De Lange HJ, Hamer M, Preuss TG, Töpke K, Maund SJ. 2011. Framework for traits-based assessment in ecotoxicology. *Integr Environl Assess Manag* 7: 172-186.

Rubach MN, Baird DJ, Boerwinkel MC, Maund SJ, Roessink I, Van Den Brink PJ. 2012.

Species traits as predictors for intrinsic sensitivity of aquatic invertebrates to the insecticide chlorpyrifos. *Ecotoxicology* 21: 2088-2101.

Ruotsalainen AM, Akkanen J, Kukkonen JJV. 2010. Dissolved organic matter modulating the uptake, biotransformation, and elimination rates of pyrene in *Daphnia magna*. *Environ Toxicol Chem* 29: 2783-2791.

Sourisseau S, Basseres A, Perieb F, Caquet T. 2008. Calibration, validation and sensitivity analysis of an ecosystem model applied to artificial streams. *Water Res* 42:1167–1181.

SCENIHR (Scientific Committee on Emerging and Newly Identified Health Risks), SCCS (Scientific Committee on Consumer Safety) and SCHER, (Scientific Committee on Health and Environmental Risks. 2013. Addressing the new challenges for risk assessment. Cited 2015-10-30. Available from:

http://ec.europa.eu/health/scientific_committees/emerging/docs/scenih_r_o_037.pdf

Stampfli NC, Knillmann S, Liess M, Beketov MA. 2011. Environmental context determines community sensitivity of freshwater zooplankton to a pesticide. *Aquatic Toxicol* 104: 116-124.

Sommer U, Gliwicz ZM, Lampert W, Duncan A. 1986. The Peg-Model of seasonal succession of planktonic events in fresh waters. *Arch Hydrobiol* 106: 433–471.

Sousa T, Domingos T, Poggiale JC, Kooijman SALM. 2010. Dynamic energy budget theory restores coherence in biology. *Philos T Roy Soc B* 365: 3413-3426.

Traas TP, Jansen JH, van den Brink PJ, Brock, TCM, Aldenberg T. 2004, A freshwater food web model for the combined effects of nutrients and insecticide stress and subsequent recovery.

Environ Toxicol Chem 23: 521–529.

- Usseglio-Polatera P, Bournaud M, Richoux P, Tachet H. 2000. Biological and ecological traits of benthic freshwater macroinvertebrates: Relationships and definition of groups with similar traits. *Freshw Biol* 43:175–205.
- Van den Brink PJ, Van Wijngaarden RPA, Lucassen WGH, Brock TCM, Leeuwangh P. 1996. Effects of the insecticide Dursban®4E (a.i. chlorpyrifos) in outdoor experimental ditches. II. Invertebrate community responses. *Environ Toxicol Chem* 15: 1143-1153.
- Van den Brink PJ, Alexander A, Desrosiers M, Goedkoop W, Goethals P, Liess M, Dyer S. 2011. Traits-based approaches in bioassessment and ecological risk assessment: strengths, weaknesses, opportunities and threats. *Int Environ Assess Manag* 7: 198-208.
- Van den Brink PJ. 2008. Ecological risk assessment: from book-keeping to chemical stress ecology. *Environ Sci Technol* 42: 8999–9004.
- Van Straalen NM. 1994. Biodiversity of ecotoxicological responses in animals. *Neth J.Zool* 44: 112-129.
- Vermeire T, Rikken M, Attias L, Boccardi P, Boeije G, de Bruijn J, Brooke D, Comber M, Dolan B, Fischer S, Heinemeyer G, Koch V, Lijzen J, Müller B, Murray-Smith R, Tadeo J. 2004. European Union System for the evaluation of substances, the second version. *Chemosphere* 59: 473–485.
- Viaene KPJ, De Laender F, Rico A, Van den Brink PJ, Di Guardo A, Morselli M, Janssen CR. 2015. Species interactions and chemical stress: Combined effects of intraspecific and interspecific interactions and pyrene on *Daphnia magna* population dynamics. *Environ Toxicol Chem* 34: 1751–1759.
- Vörösmarty CJ, Fekete BM, Meybeck M, Lammers R. 2000a. Geomorphometric attributes of the global system of rivers at 30-minute spatial resolution (STN-30). *J Hydrol* 237:17–39.

Vörösmarty CJ, Fekete BM, Meybeck M, Lammers R. 2000b. Global system of rivers: its role in organizing continental land mass and defining land-to-ocean linkages. *Global Biogeochem Cy* 14: 599–621.

Wannaz C, Fantke P, Jolliet O. 2015. Multi-scale modeling of human exposure from local source to global scale. (submitted to *Environ Sci Technol*).

Ying Z, Price OR, Tao S, Jones KC, Sweetman A. 2014. A new multimedia contaminant fate model for China: How important are environmental parameters in influencing chemical persistence and long-range transport potential? *Environ Int* 69: 18-27.